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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/588,694	11/24/2008	George R. Agnes	CDM/2353.0017	9669

152 7590 04/05/2011

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EXAMINER	
HIXSON, CHRISTOPHER	
ART UNIT	PAPER NUMBER
1777	

MAIL DATE	DELIVERY MODE
04/05/2011	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/588,694	AGNES ET AL.	
	Examiner	Art Unit	
	Christopher A. Hixson	1777	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 January 2011*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,9-35,38-42,44-54 and 56-58* is/are pending in the application.

4a) Of the above claim(s) *41* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,9-35,38-40,42,44-54,56-58* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *31 January 2011* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The applicant's amendment filed on 31 January 2011 is acknowledged. Claims 1-4, 9-35, 38-42, 44-54, and 56-58 are currently pending. Claim 41 was withdrawn and claims 5-8, 36, 37, 43, and 55 were cancelled, leaving claims 1-4, 9-35, 38-40, 42, 44-54, and 56-58 to be considered on the merits below.

Response to Amendment

2. In response to the applicant's amendment, the grounds of rejection are modified.

Drawings

3. The drawings were received on 31 January 2011. These drawings are acceptable.

Claim Rejections - 35 USC § 103

4. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

5. **Claims 1-4, 15-17, 20, 21, 23-25, 27, 29, 30, 38, 42, 44 and 45** are rejected under 35 U.S.C. 103(a) as being unpatentable over Rhim et al. (Journal of Crystal Growth 1991)(IDS)(Rhim) in view of Davis et al. (Aerosol Science and Technology 1982)(Davis) as evidenced by Lee et al. (Science 2003)(Lee), Bakhoum et al. (Analytical Chemistry 2005)(IDS)(Bakhoum) and Nilsson et al. (WO 02/057520 A1)(IDS)(Nilsson).

Regarding claim 1, Rhim teaches that he performed a method which controllably induced nucleation of a solute (abstract, where it is described that a protein crystal is grown, and in Nilsson, p.7, lines 1-10, where it is described that nucleation must be controlled in order to optimally grow a protein crystal) which included a step of providing a droplet containing the solute (p.294, "2. Electrostatic multi-drop levitator," first paragraph) levitated in an electrostatic balance. The droplet was made to acquire a charge (Id, where this must be true since droplet is charged, and and p.296, "4. Drop launch method," where droplet is created, and is described as being charged), which

lowers the mass to charge ratio of the droplet (since charging the droplet decreases the ratio m/z by definition), which controllably causes ion-induced nucleation of at least some of the solute into a condensed phase (as in Fig. 9, and in Nilsson, p.7, lines 1-10, where nucleation is part of the crystallization process, and in Lee, who teaches that charged aerosols promote nucleation).

Rhim is silent as to the mechanism for charging the droplet and does not teach that he levitated his droplet in an electrodynamic balance.

Davis teaches that charged droplets can be levitated using electrostatic or electrodynamic balances, but that electrodynamic balances are preferred since such a balance improves the ease of capturing the charged droplet when compared to electrostatic balances (p.340, col 1, first full paragraph). He furthermore indicates that he injects his droplet into the balance via a charged hypodermic needle, acting as an induction electrode, which induces the charge on the droplet (p.339, col. 2, final paragraph, where it is an induction electrode since it is an electrode by virtue of the fact that it is charged, and it is an induction electrode by virtue of the fact that it is used to induce a charge onto the droplet).

It would have been obvious to one of ordinary skill in the art at the time of invention to have modified Rhim's method to use Davis' electrodynamic balance and injection needle in order to provide a more stable apparatus to capture the charged droplet to prevent waste of precious protein material.

Regarding claims 2, 3, and 17, Rhim teaches that he adjusted the surface charge density and maintained it above a threshold value necessary to induce the onset of nucleation (p.299, col. 1, final paragraph, and where crystals were actually produced, as in Figs. 9 and 10). The ions causing the nucleation are in the outer layer of the droplet (inherent, since Bakhoum teaches that in a charged droplet, the net charge resides in the diffuse layer, and the charge in the droplet is made of ions).

Regarding claim 4, it is an inherent teaching of Rhim that the ions in the vessel in excess of the counterions induce the heterogeneous nucleation of the solute. Bakhoum teaches that excess ions acts as the nucleation site (p.3191-3192, "NaCl Nucleation and Growth in Levitated Droplets with Net Charge").

Regarding claim 15, Rhim teaches that the solution has a volatile solvent (p.297, col. 1, final paragraph and col. 2, where the solvent is allowed to evaporate) which evaporates increasing the concentration of the solute

Regarding claim 16, Rhim's solvent is evaporated leaving only the nuclei (as in Fig. 9).

Regarding claims 20, 21, and 23-25, Rhim's first solute is a solid (Fig. 9, lysozyme) and an organic molecule and a biomolecule and a protein and an organic acid.

Regarding claims 27, 29, and 30, a second solute is dissolved (p.297, "5. Protein sample," buffer salts), and both the first and second solutes are chemical compounds, and only the first protein is selectively precipitated (Fig. 9) which separates the protein from the buffer.

Regarding claim 38, Rhim differentially precipitates lysozyme over the buffer (Fig. 9).

Regarding claim 42, Rhim teaches that he performed a method which controllably induced nucleation of a solute (abstract, where it is described that a protein crystal is grown, and in Nilsson, p.7, lines 1-10, where it is described that nucleation must be controlled in order to optimally grow a protein crystal) which included a step of providing a droplet containing the solute (p.294, "2. Electrostatic multi-drop levitator," first paragraph) levitated in an electrostatic balance. The droplet was made to acquire a charge (Id, where this must be true since droplet is charged, and and p.296, "4. Drop launch method," where droplet is created, and is described as being charged), which lowers the mass to charge ratio of the droplet (since charging the droplet decreases the ratio m/z by definition), which controllably causes ion-induced nucleation of at least some of the solute into a condensed phase (as in Fig. 9, and in Nilsson, p.7, lines 1-10, where nucleation is part of the crystallization process, and in Lee, who teaches that charged aerosols promote nucleation). The precipitation was selective in that the method formed crystals of the protein (Fig. 9), but not of the buffer salts.

Rhim is silent as to the mechanism for charging the droplet and does not teach that he levitated his droplet in an electrodynamic balance.

Davis teaches that charged droplets can be levitated using electrostatic or electrodynamic balances, but that electrodynamic balances are preferred since such a balance improves the ease of capturing the charged droplet when compared to electrostatic balances (p.340, col 1, first full paragraph). He furthermore indicates that he injects his droplet into the balance via a charged hypodermic needle, acting as an induction electrode, which induces the charge on the droplet (p.339, col. 2, final paragraph, where it is an induction electrode since it is an electrode by virtue of the fact that it is charged, and it is an induction electrode by virtue of the fact that it is used to induce a charge onto the droplet).

It would have been obvious to one of ordinary skill in the art at the time of invention to have modified Rhim's method to use Davis' electrodynamic balance and injection needle in order to provide a more stable apparatus to capture the charged droplet to prevent waste of precious protein material.

Regarding claims 44 and 45, Rhim teaches that he adjusted the surface charge density and maintained it above a threshold value necessary to induce the onset of nucleation (p.299, col. 1, final paragraph, and where crystals were actually produced, as in Figs. 9 and 10). The ions causing the nucleation are in the outer layer of the droplet (inherent, since Bakhoum teaches that in a charged droplet, the net charge resides in the diffuse layer, and the charge in the droplet is made of ions).

6. **Claims 9-13, 18, and 19** are rejected under 35 U.S.C. 103(a) as being unpatentable over Rhim in view of Davis as evidenced by Lee, Bakhoum, and Nilsson as applied to claims 1-4, 15-17, 20, 21, 23-25, 27, 29, 30, 38, 42, 44, and 45 above, and further in view of Agnes et al. (WO 02/35553 A2)(IDS)(Agnes).

Regarding claim 9, Rhim's method creates the formation of at least one nuclei (Fig. 9, where at least 3 were created), and Rhim teaches that he delivers the nuclei to a target location (p.301, col. 1, collection device).

However, neither Rhim nor Davis provide evidence that such could be accomplished using the combined method involving an electrodynamic balance.

Agnes describes an electrodynamic balance which can guide a suspended droplet to an external location, such as the entrance to a mass spectrometer (abstract).

It would have been obvious to one of ordinary skill in the art at the time of invention to have substituted Agnes' electrodynamic balance with Davis' since Rhim indicates that in his method he guided his suspended crystals to a collection device, and Agnes discloses that his electrodynamic balance could accomplish this.

Regarding claims 10-13, Rhim's collection device is a substrate located away from the balance (p.301, col. 1, collection device) and at least a portion of the solution containing the nuclei is delivered, in that the charges are in the solvent.

Regarding claim 18, Rhim's method creates the formation of at least one nuclei (Fig. 9, where at least 3 were created), and Rhim teaches that he delivers the nuclei to a target location (p.301, col. 1, collection device).

However, neither Rhim nor Davis provide evidence that such could be accomplished using the combined method involving an electrodynamic balance.

Agnes describes an electrodynamic balance which can guide a suspended droplet to an external location, such as the entrance to a mass spectrometer (abstract).

It would have been obvious to one of ordinary skill in the art at the time of invention to have substituted Agnes' electrodynamic balance with Davis' since Rhim indicates that in his method he guided his suspended crystals to a collection device, and Agnes discloses that his electrodynamic balance could accomplish this.

Furthermore, Agnes teaches that droplets can include a surface tension modifier to prevent Columb explosion when using his apparatus ([0024]).

Regarding claim 19, Rhim's nuclei were used to promote crystallization (Fig. 9).

7. **Claim 14** is rejected under 35 U.S.C. 103(a) as being unpatentable over Rhim in view of Davis and Agnes as evidenced by Lee, Bakhoum, and Nilsson as applied to claims 9-13, 18, and 19 above, and further in view of Chung et al. (Journal of Crystal Growth 1998)(IDS)(Chung).

Regarding claim 14, none of the previously cited art indicates that the nuclei produced by the method seed crystal growth in a secondary vessel.

Chung describes that in a similar method, the nuclei produced seeded crystal growth in a secondary vessel (p.394, col. 1, where "hundreds of micro-crystals started forming sporadically over the next day...").

It would have been obvious to incorporate Chung's additional step of seeding crystal growth in a secondary vessel in order to produce additional crystals for study.

8. **Claims 26, 28, 33, and 34** are rejected under 35 U.S.C. 103(a) as being unpatentable over Rhim in view of Davis as evidenced by Lee, Bakhoum, and Nilsson as applied to claims 1-4, 15-17, 20, 21, 23-25, 27, 29, 30, 38, 42, 44, and 45 above, and further in view of Bogan et al. (Analytical Chemistry 2002)(IDS)(Bogan) and Medzihradszky et al. (Analytical Chemistry 2000)(Medzihradszky).

Regarding claims 26, 28, 33, and 34, none of the previously cited art teaches to nucleate CHCA or THAP.

Bogan teaches that levitated droplets containing a MALDI matrix components can be used to form solid particles of matrix and analyte for subsequent MALDI-TOF-MS analysis (p.496, col. 2, first complete paragraph).

Medzihradszky teaches that he used CHCA as a MALDI matrix (p.555, "Results and Discussion").

It would have been obvious to one of ordinary skill in the art to have modified Chung's method to co-crystallize CHCA and his solute to prepare them for a subsequent analysis.

9. **Claims 31 and 32** are rejected under 35 U.S.C. 103(a) as being unpatentable over Rhim in view of Davis, Bogan, and Medzihradszky as evidenced by Lee, Bakhoum, and Nilsson as applied to claims 26, 28, 33, and 34 above, and further in view of Julian et al. (Journal of Physical Chemistry B 2002)(IDS)(Julian).

Regarding claims 31 and 32, none of the previously cited art teaches that the method can be used for a first solute which is a stereoisomer or an enantiomer.

Julian teaches that in electrospray ionization (closely related to the method of claim 1) L- and D-serine form nuclei capable of nucleating crystallization (p.1221, col. 2, second and third complete paragraphs).

It would have been obvious to one of ordinary skill in the art at the time of invention to have made the first solute a stereoisomer or an enantiomer since Julian teaches that serine can form crystallization nuclei.

10. **Claim 35** is rejected under 35 U.S.C. 103(a) as being unpatentable over Rhim in view of Davis as evidenced by Lee, Bakhoum, and Nilsson as applied to claims 1-4, 15-17, 20, 21, 23-25, 27, 29, 30, 38, 42, 44, and 45 above, and further in view of Zaccaro et al. (Crystal Growth and Design 2001)(IDS)(Zaccaro).

None of the previously cited prior art teaches that the method can be used to selectively separate a polymorphic form of the solute.

Zaccaro teaches by passing intense pulses of laser light during crystallization, a polymorphic form of gylcine was obtained (abstract).

It would have been obvious to one of ordinary skill in the art at the time of invention to have passed a laser light through the sample at the time of crystallization in order to separate a polymorphic form of the solute in order to provide a scheme for incorporating a known procedure into the new method.

11. **Claim 39** is rejected under 35 U.S.C. 103(a) as being unpatentable over Rhim in view of Davis as evidenced by Lee, Bakhoum, and Nilsson as applied to claims 1-4, 15-17, 20, 21, 23-25, 27, 29, 30, 38, 42, 44, and 45 above, and further in view of Chung.

None of the cited prior art explicitly teaches to add a solid to the solution to further induce nucleation of his solute.

Chung indicates that this is a future direction of his research (p.395, col. 2, where he indicates that he will attempt to directly control the number and size distribution of growing crystals by using a seeding method through which small uniformly sized crystals are introduced into the levitated droplet).

It would have been obvious, then, to one of ordinary skill in the art at the time of invention to have modified the method to add a solid to the solution to further induce nucleation of the solute, since Chung indicated that adding seed crystals to his levitated droplet was an avenue he was considering pursuing to improve the quality of the crystals produced by his similar method.

12. **Claim 40** is rejected under 35 U.S.C. 103(a) as being unpatentable over Rhim in view of Davis as evidenced by Lee, Bakhoum, and Nilsson as applied to claims 1-4, 15-17, 20, 21, 23-25, 27, 29, 30, 38, 42, 44, and 45 above, and further in view of Nilsson.

None of the cited prior art explicitly teaches to optimize the ionic makeup of the solution to promote nucleation of the solute.

Nilsson indicates that the standard procedure in a crystallization experiment is to experiment with buffer solutions previously known to induced protein nucleation (p.7, lines 1-20).

It would have been obvious to one of ordinary skill in the art at the time of invention to have optimized the ionic makeup to promote nucleation since this is known as a standard procedure in protein crystallization experiments.

13. **Claims 46-50 and 58** are rejected under 35 U.S.C. 103(a) as being unpatentable over Rhim in view of Davis and Agnes as evidenced by Lee and Nilsson.

Regarding claim 46, Rhim teaches that he performed a method which controllably induced nucleation of a solute (abstract, where it is described that a protein crystal is grown, and in Nilsson, p.7, lines 1-10, where it is described that nucleation must be controlled in order to optimally grow a protein crystal) which included a step of providing a droplet containing the solute (p.294, "2. Electrostatic multi-drop levitator," first paragraph) levitated in an electrostatic balance. The droplet was made to acquire a charge (Id, where this must be true since droplet is charged, and and p.296, "4. Drop launch method," where droplet is created, and is described as being charged), which lowers the mass to charge ratio of the droplet (since charging the droplet decreases the ratio m/z by definition), which controllably causes ion-induced nucleation of at least some of the solute into a condensed phase (as in Fig. 9, and in Nilsson, p.7, lines 1-10, where nucleation is part of the crystallization process, and in Lee, who teaches that charged aerosols promote nucleation). Rhim also teaches that his balance can be programmed to guide crystals towards a collection device, separate from the balance (p.301, col. 1).

Rhim is silent as to the mechanism for charging the droplet and does not teach that he levitated his droplet in an electrodynamic balance, or that an electrodynamic balance would be capable of guiding his crystals towards a collection device.

Davis teaches that charged droplets can be levitated using electrostatic or electrodynamic balances, but that electrodynamic balances are preferred since such a

balance improves the ease of capturing the charged droplet when compared to electrostatic balances (p.340, col 1, first full paragraph). He furthermore indicates that he injects his droplet into the balance via a charged hypodermic needle, acting as an induction electrode, which induces the charge on the droplet (p.339, col. 2, final paragraph, where it is an induction electrode since it is an electrode by virtue of the fact that it is charged, and it is an induction electrode by virtue of the fact that it is used to induce a charge onto the droplet).

It would have been obvious to one of ordinary skill in the art at the time of invention to have modified Rhim's method to use Davis' electrodynamic balance and injection needle in order to provide a more stable apparatus to capture the charged droplet to prevent waste of precious protein material.

However Davis appears to remain silent as to the ability of an electrodynamic balance to guide crystals towards a collection device separate from the balance.

Agnes describes an electrodynamic balance which can guide a suspended droplet to an external location, such as the entrance to a mass spectrometer (abstract).

It would have been obvious to one of ordinary skill in the art at the time of invention to have substituted Agnes' electrodynamic balance with Davis' since Rhim indicates that in his method he guided his suspended crystals to a collection device, and Agnes discloses that his electrodynamic balance could accomplish this.

Regarding claim 47, Rhim indicates that he deposits his crystals at a predetermined target location (a collection device, as above).

Regarding claims 48 and 49, Rhim identified his crystals (as in Fig. 9 caption) which were on a substrate in a purified solid form.

Regarding claim 50, Rhim teaches that the deposition step is automated (p.301, col. 1 using keyboard commands). However, the identification of the crystals is not noted to be automated.

It is noted that to provide a mechanical or automatic means to replace manual activity, which accomplishes the same result, is within the ambit of a person of ordinary skill in the art. See In re Venner, 120 USPQ 192 (CCPA 1958) (see MPEP § 2144.04).

Regarding claim 58, Rhim teaches that he performed a method which controllably induced nucleation of a solute (abstract, where it is described that a protein crystal is grown, and in Nilsson, p.7, lines 1-10, where it is described that nucleation must be controlled in order to optimally grow a protein crystal) which included a step of providing a droplet containing the solute (p.294, "2. Electrostatic multi-drop levitator," first paragraph) levitated in an electrostatic balance. The droplet was made to acquire a charge (Id, where this must be true since droplet is charged, and and p.296, "4. Drop launch method," where droplet is created, and is described as being charged), which lowers the mass to charge ratio of the droplet (since charging the droplet decreases the ratio m/z by definition), which controllably causes ion-induced nucleation of at least some of the solute into a condensed phase (as in Fig. 9, and in Nilsson, p.7, lines 1-10, where nucleation is part of the crystallization process, and in Lee, who teaches that charged aerosols promote nucleation). Rhim also teaches that his balance can be programmed to guide crystals towards a collection device, separate from the balance (p.301, col. 1).

Rhim is silent as to the mechanism for charging the droplet and does not teach that he levitated his droplet in an electrodynamic balance, or that an electrodynamic balance would be capable of guiding his crystals towards a collection device.

Davis teaches that charged droplets can be levitated using electrostatic or electrodynamic balances, but that electrodynamic balances are preferred since such a balance improves the ease of capturing the charged droplet when compared to electrostatic balances (p.340, col 1, first full paragraph). He furthermore indicates that he injects his droplet into the balance via a charged hypodermic needle, acting as an induction electrode, which induces the charge on the droplet (p.339, col. 2, final paragraph, where it is an induction electrode since it is an electrode by virtue of the fact that it is charged, and it is an induction electrode by virtue of the fact that it is used to induce a charge onto the droplet).

It would have been obvious to one of ordinary skill in the art at the time of invention to have modified Rhim's method to use Davis' electrodynamic balance and

injection needle in order to provide a more stable apparatus to capture the charged droplet to prevent waste of precious protein material.

However Davis appears to remain silent as to the ability of an electrodynamic balance to guide crystals towards a collection device separate from the balance.

Agnes describes an electrodynamic balance which can guide a suspended droplet to an external location, such as the entrance to a mass spectrometer (abstract), by manipulation of the electric field (abstract, manipulated by electrode assembly).

It would have been obvious to one of ordinary skill in the art at the time of invention to have substituted Agnes' electrodynamic balance with Davis' since Rhim indicates that in his method he guided his suspended crystals to a collection device, and Agnes discloses that his electrodynamic balance could accomplish this.

14. **Claims 51, 52, 54, and 56** are rejected under 35 U.S.C. 103(a) as being unpatentable over Rhim in view of Davis and Agnes as evidenced by Lee, Bakhoum, and Nilsson as applied to claims 46-50 and 58 above, and further in view of Bogan and Medzihradszky.

Regarding claims 51, 52, 54, and 56, none of the previously cited art teaches to nucleate CHCA or THAP, to co-crystallize two solutes, or that the second solute is a MALDI matrix.

Bogan teaches that levitated droplets containing a mixture of inorganic and organic solutes and MALDI matrix components which can be used to form solid particles of matrix and biomolecule analytes for subsequent MALDI-TOF-MS analysis (p.496, col. 2, first complete paragraph).

Medzihradszky teaches that he used CHCA as a MALDI matrix (p.555, “Results and Discussion”).

It would have been obvious to one of ordinary skill in the art to have modified Chung’s method to co-crystallize CHCA and his solute to prepare them for a subsequent analysis.

15. **Claim 53** is rejected under 35 U.S.C. 103(a) as being unpatentable over Rhim in view of Davis, Agnes, Bogan, and Medzihradszky as evidenced by Lee, Bakhoum, and Nilsson as applied to claims 51, 52, 54, and 56 above, and further in view of Julian.

None of the previously cited prior art teaches that the method can be used for a first solute which is a stereoisomer or an enantiomer.

Julian teaches that in electrospray ionization (closely related to the method of claim 1) L- and D-serine form nuclei capable of nucleating crystallization (p.1221, col. 2, second and third complete paragraphs).

It would have been obvious to one of ordinary skill in the art at the time of invention to have made the first solute a stereoisomer or an enantiomer since Julian teaches that serine can form crystallization nuclei and this would be a useful application of the method.

16. **Claim 57** is rejected under 35 U.S.C. 103(a) as being unpatentable over Rhim in view of Davis, Agnes, Bogan, and Medzihradszky as evidenced by Lee, Bakhoum, and Nilsson as applied to claims 51, 52, 54, and 56 above, and further in view of Zaccaro.

Regarding claim 57, none of the previously cited prior art explicitly teaches that the method can be used to selectively separate a polymorphic form of the solute.

Zaccaro teaches by passing intense pulses of laser light during crystallization, a polymorphic form of gylcine was obtained (abstract).

It would have been obvious to one of ordinary skill in the art at the time of invention to have passed a laser light through the sample at the time of crystallization in order to separate a polymorphic form of the solute as a useful application of the method.

Response to Arguments

17. Applicant's arguments with respect to all claims have been considered but are moot in view of the new ground(s) of rejection.

The drawings submitted are accepted by the examiner.

The examiner withdraws the previous objection to the abstract in view of the applicant's amendment.

The examiner withdraws the previous rejection under § 112 in view of the applicant's amendment.

The examiner withdraws the previous provisional double patenting rejection in view of the applicant's amendment leading to the allowance of Application 10/399,823.

Conclusion

18. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher A. Hixson whose telephone number is (571)270-5027. The examiner can normally be reached on M-F 8 am - 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Vickie Kim can be reached on (571)272-0579. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

4/1/2011

/Yelena G. Gakh, Ph.D./
Primary Examiner, Art Unit 1777

/Christopher A. Hixson/
Examiner, Art Unit 1777